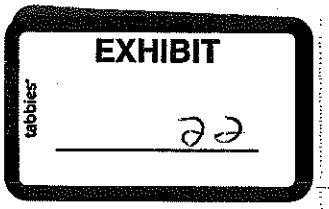
EXHIBIT 22



EVALUATION AND MANAGEMENT OF CHRONIC HEPATITIS C VIRUS (HCV) INFECTION

Federal Bureau of Prisons

Clinical Guidance

MAY 2017 (CORRECTED)

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WHAT'S NEW IN BOP GUIDANCE REGARDING HCV INFECTION?

The current corrected copy of the May 2017 contains the following correction:

- In *Appendix 11*, Note 3 has been corrected to read as follows:

  Recommended baseline testing for hepatitis B status includes HBsAg, anti-HBs, and anti-HBc. If either **HBsAg** or anti-HBc is positive, obtain an HBV DNA viral load.

The major changes included in this May 2017 update to the BOP guidance on chronic HCV infection are based primarily on the April 2017 changes to the* American Association for the Study of Liver Diseases *(AASLD) guidelines, as follows:

- The term *resistance-associated substitutions (RASs)* is now being used instead of *resistance-associated variants (RAVs)*.
- Anti-HBs and anti-HBc, in addition to HBsAg, are recommended for baseline testing of hepatitis B status (see LABORATORY TESTS under *BASELINE EVALUATION*).
- *Ledipasvir/sofosbuvir* once daily for eight weeks is now an AASLD-recommended regimen for treatment in a subgroup of HCV-infected persons who have genotype 1a or 1b, have an HCV viral load <6 million IU/ml, and are treatment-naïve—but who are not black, are not HIV-coinfected, and do not have cirrhosis.
- The treatment of peginterferon + ribavirin treatment-experienced genotype 3 with compensated cirrhosis has been updated as follows (see *APPENDIX 1*):
  - The addition of weight-based ribavirin to the sofosbuvir/velpatasvir regimen is recommended.
  - Elbasvir/grazoprevir + sofosbuvir once daily for 12 weeks is now another AASLD-recommended regimen.
- NS5A resistance testing is recommended for peginterferon + ribavirin treatment-experienced genotype 3 without cirrhosis (see *testing for RASs* under PRETREATMENT ASSESSMENT in Section 7).
  - If the Y93H RAS is present, the addition of weight-based ribavirin to a 12-week regimen of *either* daclatasvir + sofosbuvir *or* sofosbuvir/velpatasvir is recommended (see *APPENDIX 2*).
- Genotypes 5 and 6 have been added to the recommendations for treatment of HCV infection with *decompensated cirrhosis*.
- Treatment recommendations are added for cases of decompensated cirrhosis with a history of *treatment failure* using sofosbuvir or an NS5A inhibitor.
- A urine drug screen is no longer required as part of the *baseline* and *pretreatment* evaluations, and is recommended only if ongoing substance use is suspected or if it is otherwise clinically indicated.

The major changes included in the October 2016 update were as follows:

- The recommendation to test all sentenced inmates for HCV infection is clarified with a language change from a "voluntary" to an "opt out" strategy. See *Screening Criteria* in Section 2.
- *BOP Priority Criteria for HCV Treatment* have been revised and condensed into three categories: high, intermediate, and low priority. (See Section 5.)
- Pretreatment patient education—rather than informed consent—is now recommended for topics that include, but are not limited to: how to take the medication, the importance of adherence, monitoring and follow up, and potential medication side effects. When ribavirin is used, specific counseling about the risks and recommendations related to pregnancy should be provided. (See *Pregnancy* in Section 8.)

- Sofosbuvir/velpatasvir (Epclusa®), the newest FDA-approved direct acting antiviral (DAA) for HCV infection, has been incorporated into HCV treatment recommendations. It is FDA-approved for treatment of all HCV genotypes and replaces sofosbuvir + ribavirin for the treatment of genotypes 2 and 3. (See *sofosbuvir/velpatasvir* description in Section 6 and in *Appendix 9*.)
- The new formulation of paritaprevir/ritonavir/ombitasivir/dasabuvir (Viekira XR™) has been substituted for the original formulation as Viekira Pak®. Viekira XR is now preferred over Viekira Pak for use in the BOP.
- Pegylated interferon (PEG-IFN) has been eliminated from all recommended and alternative regimens except for cases of HCV genotypes 2, 3, 5, or 6 with a GFR <30 and an urgent need for treatment. (See discussion of *chronic kidney disease* in Section 8.)
- For HBV/HCV coinfection, starting treatment for HBV infection is recommended prior to or at the same time as treatment for HCV when criteria for treatment of HBV are met. When HBV treatment criteria are not met, monitoring HBV DNA levels monthly during HCV treatment is recommended. (See *HBV Coinfection* in Section 8.)
- The Appendices have been revised as necessary to reflect the above changes, including the order in which the Appendices occur.

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NOTES:

*A CTP score of **5** or **6** is considered to be compensated cirrhosis, while a score of **7** or greater is considered decompensated.*

- *Warfarin anticoagulation will invalidate CTP calculations if the INR is 1.7 or higher.*
- *It is recommended that cases of decompensated cirrhosis be managed in consultation with a clinician experienced in the treatment of this condition because the dosages of DAA medications are not well-established with severe hepatic impairment.*
- *Inmates with CTP Class C decompensated cirrhosis may have a reduced life expectancy and should be considered for Reduction In Sentence/Compassionate Release in accordance with current policy (PS 5050.49) and procedures.*

ADDITIONAL INTERVENTIONS FOR INMATES WITH CIRRHOSIS:

- **Pneumococcal vaccine:** Offer to all HCV-infected inmates with cirrhosis who are 19 through 64 years of age
  - *See the BOP Clinical Guidance on Preventive Health Care Screening.*
- **Hepatocellular carcinoma (HCC) screening:** Liver ultrasound is recommended every six months for patients with both cirrhosis *and* chronic HCV infection.
- **Esophageal varices screening:** Screening for esophageal and gastric varices with esophagogastroduodenoscopy (EGD) is recommended for patients diagnosed with cirrhosis.

Other healthcare interventions recommended for patients with cirrhosis may include:

- Nonselective beta blockers for prevention of variceal bleeding in patients with esophageal varices.
- Antibiotic prophylaxis if risk factors are present for spontaneous bacterial peritonitis.
- Optimized diuretic therapy for ascites.
- Lactulose and rifaximin therapy for encephalopathy.

In general, NSAIDs should be avoided in advanced liver disease/cirrhosis, and metformin should be avoided in decompensated cirrhosis. The detailed management of cirrhosis is beyond the scope of these guidelines. Other resources should be consulted for more specific recommendations related to this condition.

5. BOP PRIORITY CRITERIA FOR HCV TREATMENT

Determining whether BOP priority criteria for treatment are met is an important part of the initial evaluation and ongoing management of inmates with chronic HCV infection. Although all patients with chronic HCV infection may benefit from treatment, certain cases are at higher risk for complications or disease progression and require more urgent consideration for treatment. The BOP has established priority criteria to ensure that those with the greatest need are identified and treated first. The BOP Medical Director will provide periodic guidance on specific strategies for implementing these priority levels.

PRIORITY LEVEL 1 – HIGH PRIORITY FOR TREATMENT *

- ADVANCED HEPATIC FIBROSIS
  - APRI ≥ 2.0, *OR*
  - Metavir or Batts/Ludwig stage 3 or 4 on liver biopsy, *OR*
  - Known or suspected cirrhosis
- LIVER TRANSPLANT RECIPIENTS
- HEPATOCELLULAR CARCINOMA (HCC)
- COMORBID MEDICAL CONDITIONS ASSOCIATED WITH HCV, INCLUDING:
  - Cryoglobulinemia with renal disease or vasculitis
  - Certain types of lymphomas or hematologic malignancies
  - Porphyria cutanea tarda
- IMMUNOSUPPRESSANT MEDICATION FOR A COMORBID MEDICAL CONDITION
  - Some immusuppressant medications (e.g., certain chemotherapy agents and tumor necrosis factor inhibitors) may be needed to treat a comorbid medical condition, but are not recommended for use when infection is present. Although data are insufficient and current guidelines are inconsistent regarding treatment of HCV infection in this setting, such cases will be considered for prioritized treatment of HCV on an individual basis.
- CONTINUITY OF CARE FOR THOSE ALREADY STARTED ON TREATMENT, including inmates who are newly incarcerated in the BOP.

PRIORITY LEVEL 2 – INTERMEDIATE PRIORITY FOR TREATMENT *

- EVIDENCE FOR PROGRESSIVE FIBROSIS
  - APRI score ≥ 1.0
  - Stage 2 fibrosis on liver biopsy
- COMORBID MEDICAL CONDITIONS associated with more rapid progression of fibrosis
  - Coinfection with HBV or HIV
  - Comorbid liver diseases (e.g., autoimmune hepatitis, hemochromatosis, steatohepatitis)
  - Diabetes mellitus
- CHRONIC KIDNEY DISEASE (CKD) with GFR ≤ 59 mL/min per 1.73 m^2

PRIORITY LEVEL 3 – LOW PRIORITY FOR TREATMENT *

- Stage 0 to stage 1 fibrosis on liver biopsy
- APRI < 1
- All other cases of HCV infection meeting the eligibility critera for treatment, as noted below under *Other Criteria for Treatment*.

*** EXCEPTIONS to the above criteria for PRIORITY LEVELS 1–3 will be made on an individual basis and will be determined primarily by a compelling or urgent need for treatment, such as evidence for rapid progression of fibrosis, or deteriorating health status from other comorbidities.**

OTHER CRITERIA FOR TREATMENT

In addition to meeting the above criteria for Priority Levels 1–3, inmates being considered for treatment of HCV infection should:

- Have no contraindications to, or signicifant drug interactions with, any component of the treatment regimen.
- Not be pregnant, especially for any regimen that would require ribavirin or interferon.
- Have sufficient time remaining on their sentence in the BOP to complete a course of treatment.
  - *Inmates with high priority criteria (**PRIORITY LEVEL 1**), but insufficient time remaining in BOP custody, may be considered for treatment if they will have access to medications and health care providers for continuity of care at the time of release.*
- Have a life expectancy > 18 months.
- Demonstrate a willingness and an ability to adhere to a rigorous treatment regimen and to abstain from high-risk activities while incarcerated.
  - *Inmates with with evidence for ongoing high-risk behaviors, e.g., injection drug use, are considered for HCV treatment on an individual basis. Referral for evaluation and treatment of substance abuse is recommended.*

6. RECOMMENDED TREATMENT REGIMENS

Recommendations for preferred HCV treatment regimens continue to evolve, but still depend on several factors:

- **HCV GENOTYPE**
- **PRIOR HCV TREATMENT HISTORY**
- **COMPENSATED VS. DECOMPENSATED LIVER DISEASE**
- **DRUG-DRUG INTERACTIONS**

- **SPECIAL CONSIDERATIONS:** Certain conditions require special consideration when selecting an HCV treatment regimen, including decompensated cirrhosis, chronic kidney disease, solid organ transplant recipients, and pregnancy. These conditions are addressed in *Section 8*.
- **COST:** The cost of direct acting antiviral regimens can vary widely. When more than one regimen is appropriate for an individual case, the most cost-effective regimen is recommended, taking into consideration all the factors listed in the box above.

DIRECT ACTING ANTIVIRAL MEDICATIONS (DAAS)

As the name implies, these antiviral medications for HCV infection act directly on some part of the virus, usually the replication mechanism. Currently, there are three classes of HCV DAAs: polymerase inhibitors (-buvir), protease inhibitors (-previr), and NS5A replication complex inhibitors (-asvir).

- ***DAAs cannot be used as monotherapy; they must be used in combination with at least one other DAA or with ribavirin, and in some cases with peginterferon, depending on the clinical scenario.***
- ***The most commonly recommended regimens are briefly described below.*** *More detailed information about the regimens and the individual medications—including indications, contraindications, dosing and duration, and drug interactions—may be found in the Appendices.*